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(54) Title: CATERPILLER GENE FAMILY

(57) Abstract: The present invention relates to a new family of structurally and functionally related nucleic acids and proteins, designed the CATERPILLER family, which is characterized by landmark structural motifs including a nucleotide binding domain and leucine-rich repeat domains.

The published specification was used in this application

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US03/13562

A. CLASSIFICATION OF SUBJECT MATTER
IPC(7) : C12N 15/12, 15/85; C12Q 1/02; A61K 48/00
US CL : 536/23.1, 23.5; 435/29, 455; 514/44
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 536/23.1, 23.5; 435/29, 455; 514/44

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2001/0029033 A1 (SHAMI et al.) 11 October 2001 (11.10.2001), especailly Figure 7, paragraphs 0029-0035, 0037-0038, 0040-0048, 0072-0075.	1, 27, 28, 31, 32, 35, 36, 39, 40, 43
X	SHAMI et al. Identification and characterization of a novel gene that is upregulated in leukaemia cells by nitric oxide. British Journal of Haematology. January 2001, Vol. 112, No. 1, pages 138-147.	1, 27, 31, 35, 39, 43
X	Database GenBank, US National Library of Medicine (Bethesda, MD, USA), No. AF231021, SHAMI et al., 'Homo sapiens leucine-rich-repeat protein RNO2 mRNA, complete cds., 02 March 2001.	1
X	PHILLIPS et al. Expression of rno-2 inhibits growth and induces differentiation and apoptosis in leukemia cells. Blood. 16 November 2001, Vol. 98, No. 11 part 2, page	27, 28, 31, 32, 35, 36, 39, 40, 43
P, X	US 2003/0027757 A1 (BERTIN et al.) 06 February 2003 (06.02.2003), see entire reference relating to PYRIN-8, especially Figure 8; paragraphs 0010-0013, 0018-0023, 0027, 0064-0069, 0087, 0092-0093, 0114, 0135-0138, 0150, 0153-0161, 0176-0177, 0251-0277, and 0397; claims 1-7, 19-20.	1, 3, 27, 28, 31, 32, 35, 36, 39, 40, 43, 44
P, A	SRINIVASULA et al. The PYRIN-CARD protein ASC is an activating adapter for Caspase-1. Journal of Biological Chemistry. 14 June 2002, Vol. 277, No. 24, pages 21119-21122.	1, 3, 27, 28, 31, 32, 35, 36, 39, 40, 43, 44

☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"B" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

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PCT/US03/13562

INTERNATIONAL SEARCH REPORT

C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, A	TSCHOPP et al. NALPS: a novel protein family involved in inflammation. Nature Reviews: Molecular Cell Biology. February 2003, Vol. 4, No. 2, pages 95-104.	1, 3, 27, 28, 31, 32, 35, 36, 39, 40, 43, 44
P, X	WANG et al. PYPAF7, a novel PYRIN-containing Apaf1-like protein that regulates activation of NF-kappaB and caspase-1-dependent cytokine processing. Journal of Biological Chemistry. 16 August 2002, Vol. 277, No. 33, pages 29874-29880, see entire reference.	1, 3, 27, 28, 31, 32, 35, 36, 39, 40, 43
P, X	Database GenBank, US National Library of Medicine (Bethesda, MD, USA), No. NM_033297, TSCHOPP et al., 'Homo sapiens neuronal apoptosis inhibitor protein 12 (NALP12), mRNA', 18 April 2003.	1, 3
T	WILLIAMS et al. Cutting edge: Monarch-1: a pyrin/nucleotide-binding domain/leucine-rich repeat protein that controlls classical and nonclassical MHC class I genes. Journal of Immunology. June 2003, Vol. 170, No. 11, pages 5354-5358, see entire reference.	1, 3, 27, 28, 31, 32, 35, 36, 39, 40, 43

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INTERNATIONAL SEARCH REPORT

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Groups I-VI, claim(s) 1-3, 27, 28, 31, 32, 35, 36, 39, 40, 43, and 44, drawn to an isolated nucleic acid encoding a polypeptide selected from: Monarch-1 polypeptide (group I); CATERPILLER 11.2 polypeptide (group II); CATERPILLER 11.3 polypeptide (group III); CATERPILLER 16.1 polypeptide (group IV); CATERPILLER 16.2 polypeptide (group V); and CIAS1 polypeptide (group VI), and the first recited method of using same in a method for modulating activity of the selected polypeptide in a cell, including modulating cellular inflammatory responses, apoptosis, and Toll-like receptor activity. Claim 2 is included only in Group VI. .

Groups VII-XII, claim(s) 27, 29, 31, 33, 35, 37, 39, 41, 43, and 44, drawn to a method for modulating activity of a polypeptide selected from: Monarch-1 polypeptide (group VII); CATERPILLER 11.2 polypeptide (group VIII); CATERPILLER 11.3 polypeptide (group IX); CATERPILLER 16.1 polypeptide (group X); CATERPILLER 16.2 polypeptide (group XI); and CIAS1 polypeptide (group XII), in a cell using an antisense oligonucleotide that targets the cellular nucleic acid encoding the selected polypeptide, including modulating cellular inflammatory responses, apoptosis, and Toll-like receptor activity.

Groups XIII-XVIII, claim(s) 27, 29, 31, 33, 35, 37, 39, 41, 43, and 44, drawn to a method for modulating activity of a polypeptide selected from: Monarch-1 polypeptide (group XIII); CATERPILLER 11.2 polypeptide (group XIV); CATERPILLER 11.3 polypeptide (group XV); CATERPILLER 16.1 polypeptide (group XVI); CATERPILLER 16.2 polypeptide (group XVII); and CIAS1 polypeptide (group XVIII), in a cell using a siRNA that targets the cellular nucleic acid encoding the selected polypeptide, including modulating cellular inflammatory responses, apoptosis, and Toll-like receptor activity.

Groups XIX-XXIV, claim(s) 27, 30, 31, 34, 35, 38, 39, and 42-44, drawn to a method for modulating activity of a polypeptide selected from: Monarch-1 polypeptide (group XIX); CATERPILLER 11.2 polypeptide (group XX); CATERPILLER 11.3 polypeptide (group XXI); CATERPILLER 16.1 polypeptide (group XXII); CATERPILLER 16.2 polypeptide (group XXIII); and CIAS1 polypeptide (group XIV), in a cell using an antibody that binds the selected polypeptide, including modulating cellular inflammatory responses, apoptosis, and Toll-like receptor activity.

Groups XXV-XXX, claim(s) 45-52, drawn to a cell-based method for identifying a compound that binds to or modulates the activity of a polypeptide selected from: Monarch-1 polypeptide (group XXV); CATERPILLER 11.2 polypeptide (group XXVI); CATERPILLER 11.3 polypeptide (group XXVII); CATERPILLER 16.1 polypeptide (group XXVIII); CATERPILLER 16.2 polypeptide (group XXIX); and CIAS1 polypeptide (group XXX), which is the second recited method of using a nucleic acid encoding the selected polypeptide of groups I-VI, respectively.

Groups XXXI-XXXVI, claim(s) 45-49 and 53, drawn to a cell-free method for identifying a compound that binds to or modulates the activity of a polypeptide selected from: Monarch-1 polypeptide (group XXXI); CATERPILLER 11.2 polypeptide (group XXXII); CATERPILLER 11.3 polypeptide (group XXIII); CATERPILLER 16.1 polypeptide (group XXXIV); CATERPILLER 16.2 polypeptide (group XXXV); and CIAS1 polypeptide (group XXXVI).

Groups XXXVII-XLII, claim(s) 45-49 and 54, drawn to a transgenic non-human mammal-based method for identifying a compound that binds to or modulates the activity of a polypeptide selected from: Monarch-1 polypeptide (group XXXI); CATERPILLER 11.2 polypeptide (group XXXII); CATERPILLER 11.3 polypeptide (group XXIII); CATERPILLER 16.1 polypeptide (group XXXIV); CATERPILLER 16.2 polypeptide (group XXXV); and CIAS1 polypeptide (group XXXVI), which is the third recited method of using a nucleic acid encoding the selected polypeptide of groups I-VI, respectively.

The inventions listed as Groups I-XLII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Under 37 CFR 1.475(b) and (d), the International Searching Authority does not recognize unity of invention between multiple different products that do not share a special technical feature or between multiple different methods of using a product.

INTERNATIONAL SEARCH REPORT

Monarch-1, CATERPILLER 11.2, CATERPILLER 11.3, CATERPILLER 16.1, CATERPILLER 16.2, and CIAS1 are different proteins having different structures and biological functions. The special technical feature of nucleic acids encoding each of these polypeptides is the sequence of the nucleic acids themselves with respect to the polypeptide each encodes. As disclosed in the description, these polypeptides are different members of a protein family, members of which were known in the prior art.

Groups I-VI include the polynucleotide encoding each of these polypeptides, respectively, and the first recited method of using each in a method of treating cells that results in modulation of the activity of the polypeptide in the cell and the consequent modulation of cellular process. Groups XXV-XXX are directed to a different use of the polynucleotides in making cells that expresses the polypeptides encoded by the polynucleotides, and then using the cells in assays to identify compounds that modulate the activity of the polypeptides. Groups XXXVII-XLII are directed to another different use of the polynucleotides in making transgenic non-human mammals that comprise the nucleic acids, and then using the cell in an assay to identify compounds that modulate the activity of the polypeptide encoded by the nucleic acids. Groups XXV-XXX and Groups XXXVII-XLII constitute the second and third use for the nucleic acids of Groups I-VI, and under 37 CFR 1.475 (d) constitute different inventions.

Groups VII-XII, groups XIII-XVIII and groups XIX-XXIV are directed to different methods for modulating the activity of one of Monarch-1, CATERPILLER 11.2, CATERPILLER 11.3, CATERPILLER 16.1, CATERPILLER 16.2, and CIAS1 polypeptides, where each set of groups uses a different type of compound: antisense oligonucleotides, siRNA or antibodies, respectively. Each of these types of compounds are structurally different from one another and operate by different mechanisms to modulate the activity of the corresponding polypeptide. Since the methods do not use the same types of compound they do not share the same special technical feature. These groups do not share a special technical feature with the nucleic acid of groups I-VI, since the nucleic acids are not used in the methods of these groups.

Groups XXXI-XXXVI are directed to a method that has a different purpose than do the methods of groups I-XXX and XXVII-XLII, and does not use the same products as in these groups. As a result, it does not share a technical feature, whether special or not, with groups I-XXX and XXVII-XLII.

Continuation of B. FIELDS SEARCHED Item 3:
MEDLINE, EMBASE, BIOSIS, CAPLUS, SCISEARCH, USPT, PGPB, DWPI, GENBANK, GENESEQ, PIR, SWISSPROT, SPTREMBL
search terms: SEQ ID NO: 2, Monarch-1, NALP12, PYPAF7, Pyrin-8, Rno-1, Rno-2

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US03/13562

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claim Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☒ Claim Nos.: 4-26
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1,3,27,28,31,32,35,36,39,40,43 and 44

Remark on Protest
☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.